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Original article

Maternal dietary patterns during pregnancy and offspring cardiometabolic health at age 6 years: The generation R study

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SUMMARY

Background & aims: Maternal nutrition during pregnancy might be important in influencing offspring cardiometabolic health. However, research has focused mostly on specific nutrients or total energy, and possible effects of whole diet are unclear. We aimed to assess the associations between different dietary patterns during pregnancy and offspring cardiometabolic health among 2592 mother–child pairs from Generation R, a prospective population-based cohort study from fetal life onwards in Rotterdam, the Netherlands.
Methods: Maternal diet was assessed in early pregnancy with a food-frequency questionnaire. We identified three *a posteriori*-dietary patterns, namely a 'Vegetable, fish and oil', 'Nuts, soy and high-fiber cereals' and 'Margarine, snacks and sugar'-pattern. An *a priori*-pattern was created based on the 'Dutch Healthy Diet Index'. Cardiometabolic health (pulse wave velocity, blood pressure, insulin, HDL-cholesterol and triglycerides) was measured at the child's age of 6 years.
Results: In the crude models, the 'Vegetable, fish and oil', 'Nuts, soy and high-fiber cereals' and 'Dutch Healthy Diet Index' seemed beneficial, as higher adherence to these patterns was significantly associated with lower blood pressure and lower pulse wave velocity. After adjustment for other socio-demographic and lifestyle factors, most associations disappeared, except for lower pulse wave velocity with the 'Vegetable, fish and oil'-dietary pattern (−0.19 SD (95% CI −0.33; −0.06), highest quartile of adherence vs. lowest quartile). No associations were found between maternal dietary patterns and offspring blood lipids or insulin levels.
Conclusions: Our results suggest that there are no consistent independent associations of maternal dietary patterns with offspring cardiometabolic health at 6 years.
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1. Introduction

Cardiometabolic diseases in adults have been linked to exposures during early life [1]. One of the consequences of malnutrition during pregnancy is low birth weight, and this may predispose higher risk of cardiometabolic diseases later in life [2,3]. However, the Hungerwinter study showed that maternal malnutrition was associated with offspring health without affecting size at birth [4]. In addition, micronutrient status during pregnancy has been related to cardiometabolic outcomes in the offspring, also independent of child's birth weight [5]. This suggests that total energy intake and fetal growth restriction are not the only pathways in predisposing these children to a higher risk of chronic disease, but that a direct effect of maternal diet might exist [6,7].

Severe energy restriction during pregnancy is suggested to influence offspring health [2]. However, what the optimal diet is during pregnancy for adequate child health is still an unresolved

Abbreviations: BF%, body fat percentage; DHD-index, Dutch healthy diet index; DBP, diastolic blood pressure; DXA, dual-energy X-ray absorptiometry; FFQ, food-frequency questionnaire; HDL-c, HDL cholesterol; ICC, intraclass correlation coefficients; PCA, principal component analysis; PWV, pulse wave velocity; SFA, saturated fat; SD, standard deviation; SDS, standard deviation score; SBP, systolic blood pressure; TFA, transfat.

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question [8]. In addition, human studies on intrauterine exposures and later cardiometabolic health mainly focused on birth weight, and studies on the role of maternal diet are scarce and inconsistent [8,9].

Last decades, research in nutritional epidemiology started focusing on overall diet instead of individual nutrients or foods, to take the interactions within diet into account [10,11]. Furthermore, studies based on dietary patterns are helpful in translating results from nutritional epidemiology to food-based dietary guidelines [12].

A priori-dietary patterns are usually defined based on dietary guidelines and expert advice, and thus generally reflect a diet that is related to health outcomes [10]. *A posteriori*-dietary patterns are data-driven and thus reflect actual dietary patterns within specific study populations. We examined the associations of different types of *a posteriori* and a priori-defined dietary patterns during pregnancy with cardiometabolic health in offspring at the age of 6 years.

2. Materials and methods

2.1. Design

The present study was embedded within the Generation R Study, a population-based cohort study from fetal life onwards that has been previously described in detail [13]. The study was conducted following the World Medical Association Declaration of Helsinki and was approved by the Medical Ethics Committee at Erasmus University Medical Center. Written consent was obtained from all participants.

2.2. Population

A flowchart of the selection process of the study population is shown in Fig. 1. Since cultural differences could influence dietary patterns and the food-frequency questionnaire (FFQ) was designed for a Dutch population, we included only mothers of Dutch national origin. Dietary patterns were determined in the 3479 mothers with dietary data available and a singleton live birth. At the child's age of 6 years, 2689 children visited the research center. Since not all children had all measurements done, population for analysis ranged from 1710 to 2548 (Fig. 1).

2.3. Dietary assessment

Diet in early pregnancy (median 13.4 weeks of gestation, 95%-range 9.9–22.8) was assessed with an adapted version of the semi-quantitative 170-item FFQ from Klipstein-Grobusch et al. [14]. In addition, for the purpose of this study, the FFQ was complemented with additional food items and the final FFQ consisted of 293 food items. This FFQ was validated with three 24 h-recalls in a group of Dutch pregnant women in Rotterdam (n = 71), who were visiting the community midwife practices. The intraclass correlation coefficients (ICCs) for energy-adjusted macronutrient intake were between 0.48 and 0.68 (unpublished data).

2.4. A priori-dietary patterns

An *a priori*-dietary pattern was defined based on the previously constructed 'Dutch Healthy Diet Index' (DHD-index) developed by van Lee et al. [15]. The DHD-index comprises of ten components: physical activity, vegetable, fruit, dietary fiber, fish, saturated fat (SFA), trans-fat (TFA), consumption occasions with acidic drinks and foods sodium and alcohol, which represent the 2006 Dutch dietary guidelines [16]. For the purpose of this study, we omitted the components 'physical activity', 'consumption of acidic drinks and foods' and 'TFA' since this data was not collected during pregnancy.

We also excluded the alcohol component, because women who consume one unit of alcohol per day would still receive the maximum score for the DHD-index, while during pregnancy any alcohol consumption is discouraged because of the known adverse effects on the fetus [17].

The scores for the remaining six DHD-index components ranged between 0 and 10 points, resulting in a total summed score ranging between 0 and 60 points. Higher scores correspond to a higher level of adherence to the Dutch dietary guidelines and therefore a healthier diet.

2.5. A posteriori-dietary patterns

Principal Component Analysis (PCA) [11] was used in order to determine *a posteriori*-dietary patterns. First, the 293 individual food items were reduced to 23 food groups (Table 1). This division was based on the Dutch National Food Consumption Survey classification [18], but some adjustments towards this division have been made in order to better capture specific nutrients (e.g. dividing cereals into low and high-fiber cereals). All factors (i.e. dietary patterns) with an eigenvalue of ≥1.5 were extracted. To improve interpretation of the dietary patterns, the Varimax rotation was used [19]. Subsequently, a factor loading was calculated for each single food group, which illustrates the extent to which each food group is correlated with the specific dietary pattern. The three highest factor loadings per dietary pattern were used to label the dietary pattern (Table 1). For each mother, regression-based scores were extracted and used as adherence scores for these dietary patterns. Subsequently, the adherence scores of the population for analysis (n = 2695) were categorized into quartiles.

2.6. Cardiometabolic risk factors

At age 6 years, all children were invited to our dedicated research facility at the Sophia's Children Hospital. While the children were lying, systolic and diastolic blood pressure (SBP and DBP) were measured at the right brachial artery for four times with one-minute intervals, using the validated automatic phygmomanometer Datascope Accutor Plus TM (Paramus, NJ, USA). Mean SBP and DBP were calculated, with exclusion of the first measurement. Carotid-femoral pulse wave velocity (PWV) was assessed using the automatic Complior SP device (Complior; Artech Medical, Pantin, France) with participants in supine position. Non-fasting blood samples were drawn by antecubital venipuncture. Insulin, HDL cholesterol (HDL-c), and triglyceride concentrations were measured with enzymatic methods (using a Cobas 8000 analyzer, Roche, Almere, The Netherlands). Quality control samples demonstrated intra-assay and inter-assay coefficients of variation ranging from 0.69 to 1.57%. Body fat was measured by Dual-energy X-ray absorptiometry (DXA) scans (iDXA; General Electric, 2008, Madison, WI, USA). Percentage body fat (BF%) was calculated as 100%* [total body fat mass(g)]/[total body mass (fat mass + lean mass + bone mass) (g)]. Body fat percentage was analyzed as part of a separate study focused on body composition, and is therefore not presented. Age- and sex-specific SD scores were created for all outcomes based on the total Generation R population with available measurements. Insulin was not normally distributed and was therefore transformed with square root transformation before standardizing.

In addition to the individual cardiometabolic outcomes, we calculated a continuous cardiometabolic risk factor score. Following examples of previously defined metabolic syndrome scores for children [20], we included BF%, blood pressure (including DBP and

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